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L4	Langedijlk P.in.	0	L4
L3	Langedijlk J.in.	0	L3
L2	-L1	114389	L2
L1	Landedijk J.in.	0	L1

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L4	Langedijlk P.in.	0	L4
L3	Langedijlk J.in.	0	L3
L2	-L1	114389	L2
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1: Virology 1994 Feb;198(2):653-62

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Loss of conserved cysteine residues in the attachment (G) glycoprotein of two human respiratory syncytial virus escape mutants that contain multiple A-G substitutions (hypermutations).

Rueda P, Garcia-Barreno B, Melero JA.

Centro Nacional de Microbiologia, Instituto de Salud Carlos III, Majadahonda, Madrid, Spain.

Two escape mutants (R10c/1 and R10c/10) of the human respiratory syncytial (RS) virus Long strain were selected after serial passage in the presence of monoclonal antibody c793 directed against the G glycoprotein. This antibody recognizes an epitope which is shared by all viruses of the two antigenic subgroups in which human RS virus isolates have been subdivided. The mutant viruses had lost most of the G protein conserved and subgroup-specific epitopes but maintained the strain-variable epitopes. The two mutants had 10 or 11 nucleotide changes in the central region of the G protein gene when compared to the Long sequence, and almost all of those changes were different between the two mutants. The majority of the nucleotide changes involved A-G transitions (U-C in the positive sense) that resulted in amino acid substitutions. Each mutant had a total of six amino acid changes, and the changes were different between the two mutants. Unexpectedly, each mutant lost one of the four conserved cysteines of the G protein, and a different cysteine (Cys 182 or 186) was lost in each mutant. They are, in fact, the first reported RS viruses with only three cysteines in the G protein ectodomain. The genetic mechanism that generated the escape mutants and its relevance for the natural history of RS virus are discussed.

PMID: 7507282 [PubMed - indexed for MEDLINE]

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L1	Gorman J.in.	64	L1

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1: J Gen Virol 1997 Oct;78 (Pt 10):2419-29 Related Articles, NEW Links

Antigenic structure of the human respiratory syncytial virus G glycoprotein and relevance of hypermutation events for the generation of antigenic variants.

Martinez I, Dopazo J, Melero JA.

Centro Nacional de Biologia Fundamental, Instituto de Salud Carlos III, Majadahonda, Madrid, Spain.

A set of monoclonal antibodies (MAbs) specific for the attachment (G) glycoprotein of a recently isolated strain of human respiratory syncytial virus (HRSV) is described. Antibody reactivity with a series of HRSV isolates belonging to antigenic groups A and B identified three epitope categories: (i) strain-specific or variable epitopes that were present in a limited set of viruses from the same antigenic group, (ii) group-specific epitopes shared by viruses from the same antigenic group and (iii) conserved epitopes present in all HRSV isolates. Sequence analysis of escape mutants was used to map relevant antigenic sites of the G glycoprotein. Strain-specific epitopes were located preferentially in the variable C-terminal third of the G polypeptide, in agreement with previous studies of the Long strain. However, a new strain-specific epitope was mapped into another variable region, N-terminal to the cluster of cysteines in the G protein ectodomain. In contrast, the group-specific and conserved epitopes were located in the central conserved region of the G protein primary structure. These results, together with previous analysis of the Long strain, provide a detailed antigenic map of the HRSV attachment protein. Some mutants selected with group-specific antibodies contain multiple A-G substitutions (hypermutations) and lack one or two of the four cysteines which are conserved in all HRSV isolates. The genetic mechanism implicated in the generation of the hypermutated viruses and its relevance for the natural history of HRSV are discussed.

PMID: 9349460 [PubMed - indexed for MEDLINE]

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1: Virus Res 1994 Sep;33(3):203-17 Related Articles, NEW! Links

Genetic heterogeneity of the attachment glycoprotein G among group A respiratory syncytial viruses.

Sanz MC, Kew OM, Anderson LJ.

Department of Molecular Biology, Biokit S.A., Barcelona, Spain.

Fifteen independent group A respiratory syncytial virus (RSV) isolates were compared by sequencing a 300-nucleotide interval encoding a variable region of the attachment glycoprotein G. The viruses compared included the reference strains Long (USA 1956), A2 (Australia 1961), and 669 (Sweden 1959), along with 13 clinical isolates obtained at different times and locations throughout the United States. Representatives of all six antigenic subgroups, recognized by reactivity patterns with monoclonal antibodies, were compared. The maximum sequence heterogeneity within the G glycoprotein region compared was 15.7% of nucleotide sequences and 26% of amino acid sequences, more than twice the difference observed between Long and A2. Half of the nucleotide changes encoded amino acid substitutions, possibly indicating that the protein interval compared was subject to immune selection. Because the ratio of nucleotide to amino acid substitutions was nearly constant for all degrees of genetic divergence, the potential range of sequence divergence among group A RSV has probably not yet been attained. There was little correlation between the patterns of reactivity against a panel of monoclonal antibodies and sequence relationships among the 15 isolates. The sequence information showed multiple genotypes circulating simultaneously in the same community and very similar genotypes circulating in widely separated communities and during different years. Genetic analyses of RSV strains can provide important information about the relationships between RSV infections.

PMID: 7985408 [PubMed - indexed for MEDLINE]

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L1	Binz H.in.	12	L1

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